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GENOVA | 21-22 novembre 2024

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La ART durante le Infezioni Opportunistiche: scelte terapeutiche e timing

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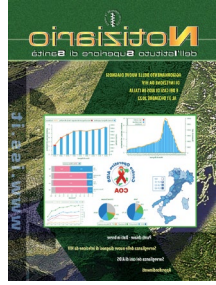
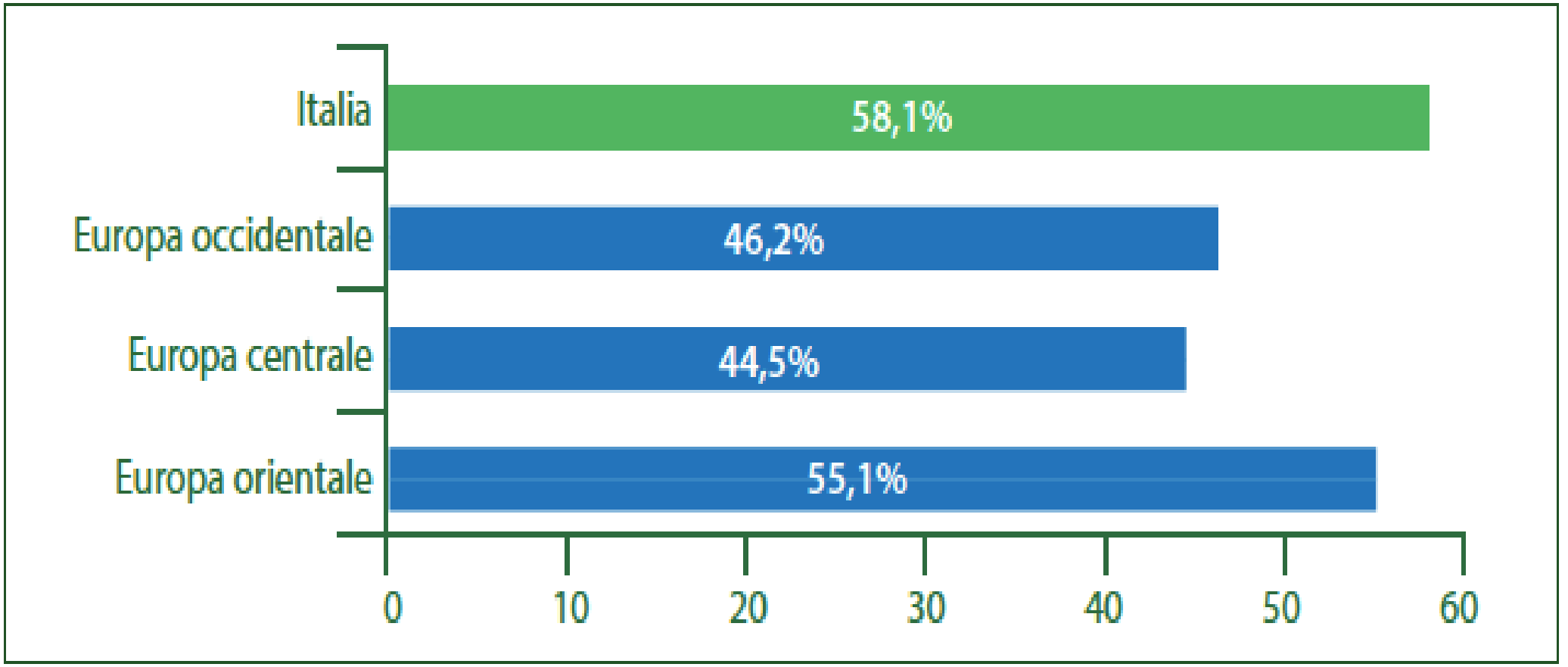


*Late presenters** 2022



(*) *Late presenters*: nuove diagnosi di infezione da HIV con numero di linfociti CD4 <350 cell/µl.

Fonti: Sistema di Sorveglianza HIV nazionale, *ECDC/WHO. HIV/AIDS Surveillance in Europe 2023-2022 data (1)*

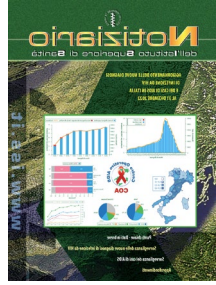
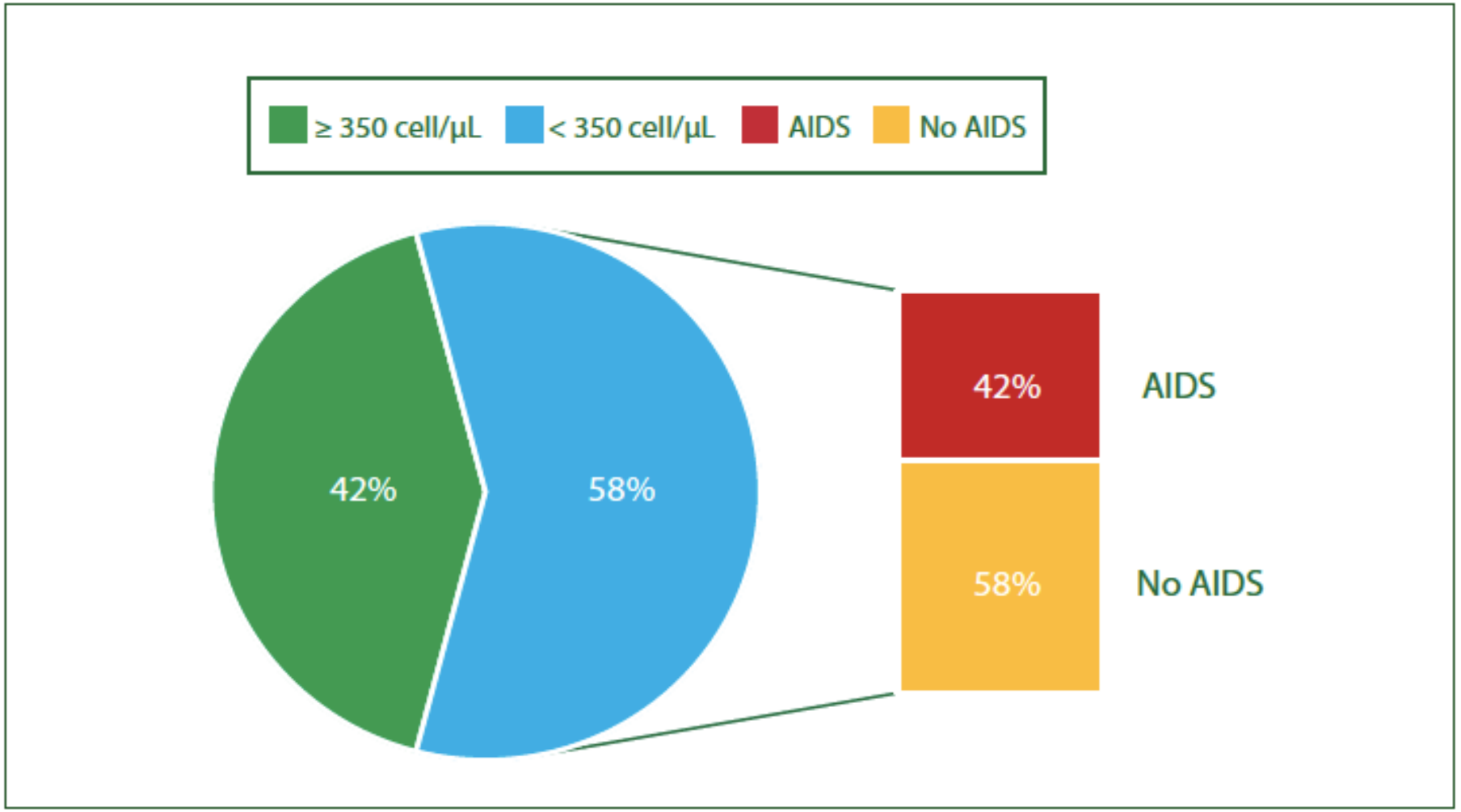
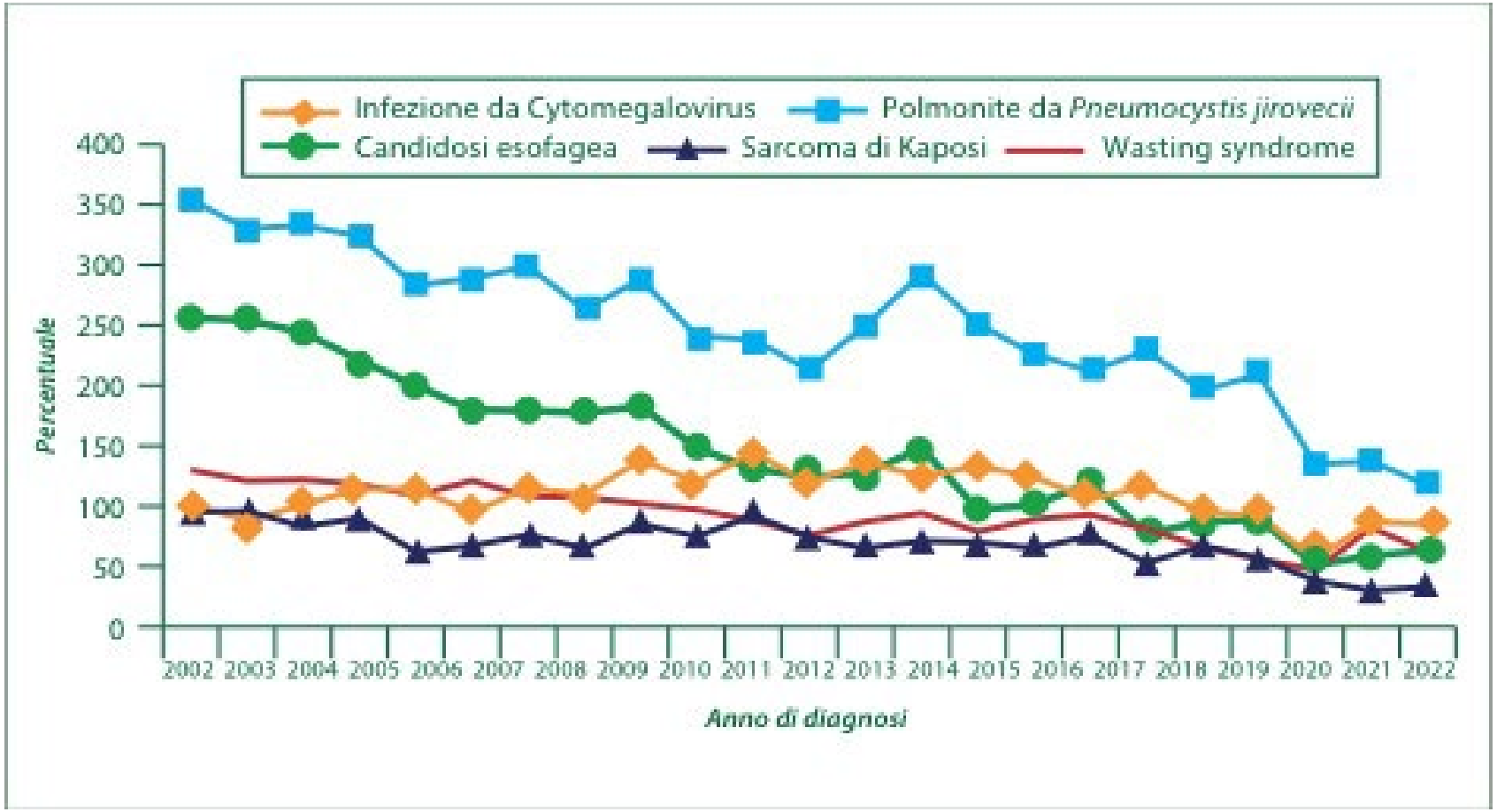


Figura 12 - Proporzione delle nuove diagnosi di infezione da HIV per numero di linfociti CD4 e diagnosi di AIDS (2022)



Nel 2022 si sono registrate 403 nuove diagnosi di AIDS, pari a un'incidenza di 0,7 casi per 100.000 residenti.
La maggior parte delle persone (83,7%) che hanno ricevuto una diagnosi di AIDS ha scoperto la propria sieropositività da meno di 6 mesi, tempo intercorso tra il primo test HIV positivo e la diagnosi di AIDS.

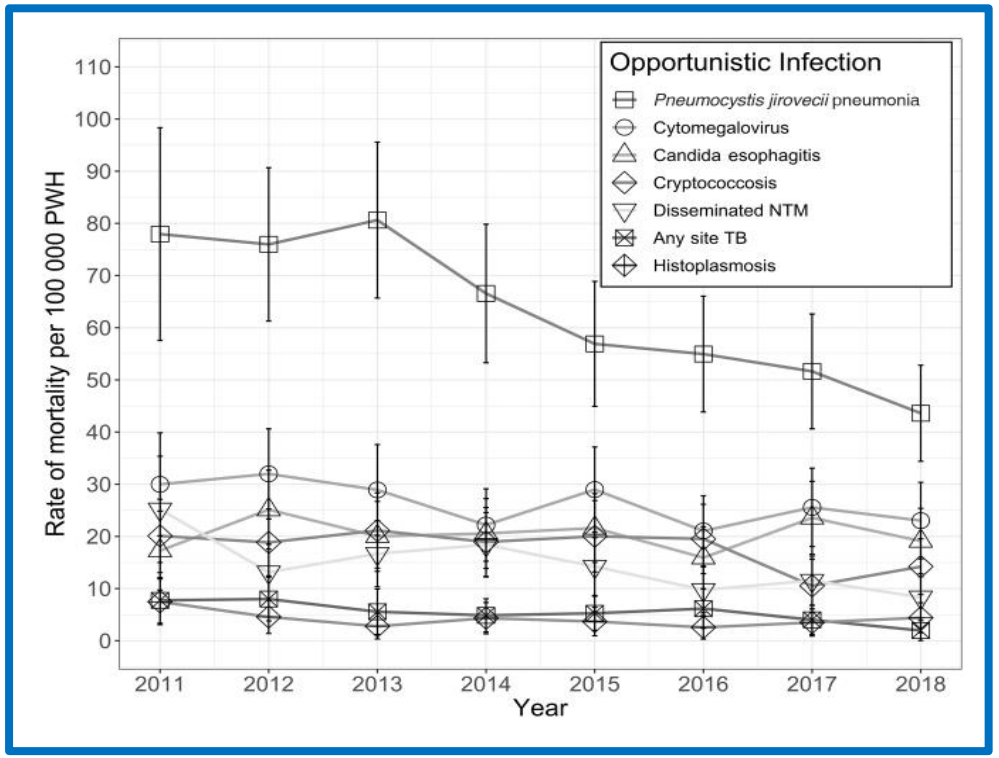
Andamento temporale delle più comuni patologie indicative di AIDS in persone che non hanno effettuato trattamenti antiretrovirali pre-AIDS (2000-2022)



National Hospitalization Rates and In-Hospital Mortality Rates of HIV–Related Opportunistic Infections in the United States, 2011–2018

Clinical Infectious Diseases
MAJOR ARTICLE

Study design: all OI-related US hospitalization rates and in-hospital mortality per 100 000 PWH were estimated for the years 2011 through 2018



Variable	OI-Related Hospitalizations, No. (Column %)	In-Hospital Mortality (Row %)	In-Hospital Mortality, No. (Column %)	Alive at Discharge, No. (Column %)	*P* Value[a]
Total	154 429	6.0	9336	145 094	
Year					>.9
2011	23 165 (15.0)	5.9	1371 (14.7)	21 794 (15.0)	
2012	20 870 (13.5)	6.1	1280 (13.7)	19 590 (13.5)	
2013	20 505 (13.3)	6.1	1245 (13.3)	19 260 (13.3)	
2014	19 805 (12.8)	6.0	1180 (12.6)	18 625 (12.8)	
2015	18 480 (12.0)	6.3	1160 (12.4)	17 320 (11.9)	
2016	17 720 (11.5)	6.0	1065 (11.4)	16 655 (11.5)	
2017	17 075 (11.1)	6.2	1050 (11.2)	16 025 (11.0)	
2018	16 810 (10.8)	5.9	985 (10.6)	15 825 (10.9)	

The OI-related hospitalization rate fell from 2725.3 (95% CI, 2266.9–3183.7) per 100000 PWH in 2011 to 1647.3 (95% CI, 1492.5–1802.1) in 2018 (*P*?.001), but the proportion of hospitalizations with mortality was stable (5.9% in 2011 and 2018).
Higher OI-related mortality was associated with older age (LR *P*?.001), male sex (LR *P*?.001), Hispanic race/ ethnicity (LR *P*?.001), and being uninsured (LR *P*?.009).

Variable Impact on Mortality of AIDS-Defining Events Diagnosed during Combination Antiretroviral Therapy: Not All AIDS-Defining Conditions Are Created Equal

31620 pts from 15 cohorts (ART-CC): during a median follow-up period of 43 months, 2880 ADEs were diagnosed in 2262 patients; 1146 patients died

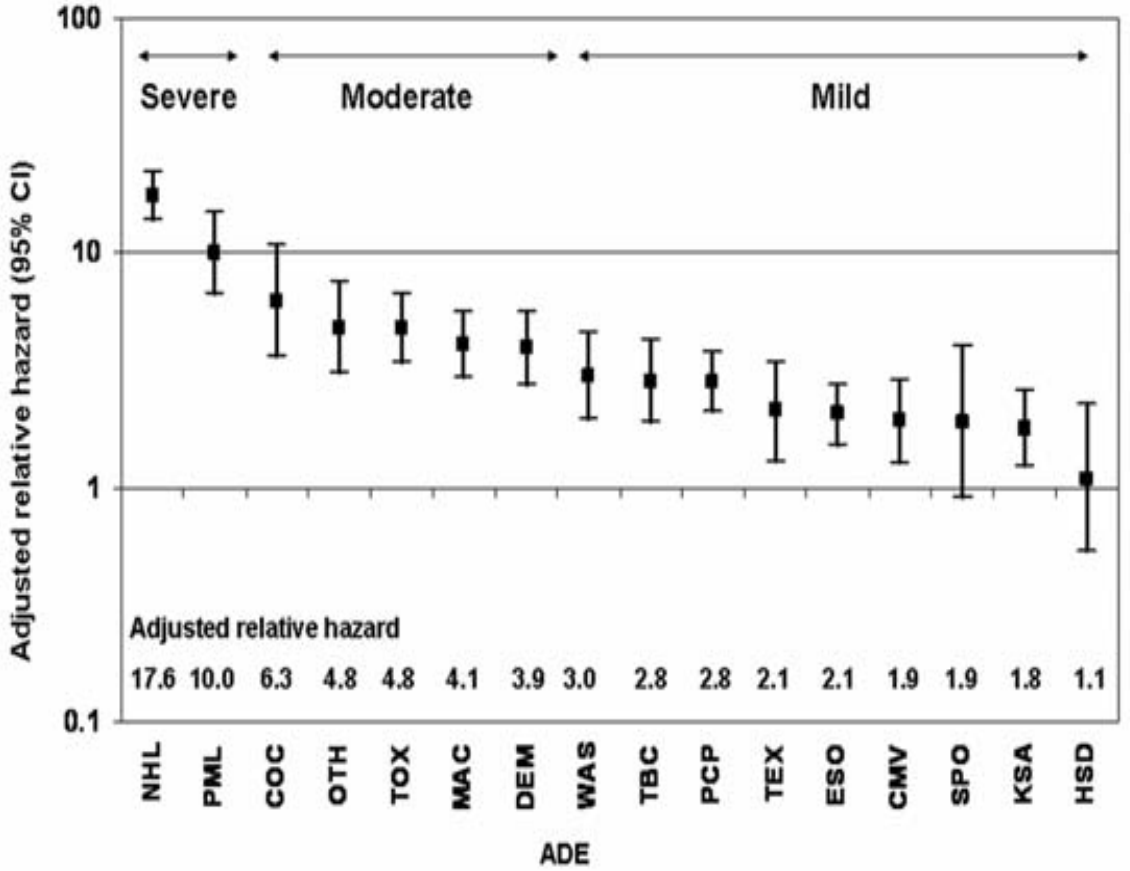
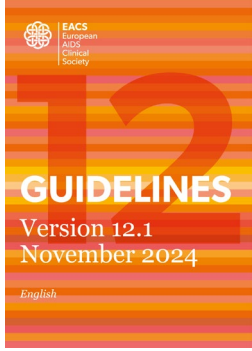


Table 2. Ranking and classification of AIDS-defining events (ADEs) according to severity (impact on subsequent mortality) in antiretroviral-naive patients initiating combination antiretroviral therapy.

ADE	Median rank (2.5th and 97.5th percentiles)	ADE severity category
Non-Hodgkin's lymphoma	16 (15–16)	Severe
Progressive multifocal leukoencephalopathy	15 (13–16)	Severe
Cryptococcosis	14 (8–15)	Moderate
Cerebral toxoplasmosis	12 (6–14)	Moderate
Rare ADE[a]	12 (8–14)	Moderate
AIDS dementia complex	11 (6–14)	Moderate
Disseminated *Mycobacterium avium* disease	11 (6–14)	Moderate
HIV wasting syndrome	8 (2–13)	Mild
Pulmonary tuberculosis	7 (3–12)	Mild
Pneumocystis jiroveci (carinii) pneumonia	7 (3–11)	Mild
Extrapulmonary tuberculosis	5 (1–10)	Mild
Esophageal candidiasis	5 (2–9)	Mild
Cryptosporidiosis	4 (1–12)	Mild
Cytomegalovirus infection	4 (1–9)	Mild
Kaposi sarcoma	3 (1–8)	Mild
Herpes simplex disease	1 (1–8)	Mild

When to start ART in persons with Opportunistic Infections



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General recommendation	As soon as possible within 2 weeks after starting treatment for the opportunistic infection	
TB meningitis	In persons with CD4 < 50 cells/μL, ART should be initiated within the first 2 weeks after initiation of TB treatment, if close monitoring and optimal TB treatment can be ensured ART initiation should be delayed for 4 weeks in all other cases	Corticosteroids are recommended as adjuvant treatment. For further discussion see Diagnosis and Treatment of TB in Persons with HIV Earlier ART start in selected patients could be considered in settings where very close monitoring and optimal treatment are available
Cryptococcal meningitis	Delay ART initiation for 4-6 weeks	Corticosteroids are **not** recommended as adjuvant treatment Earlier ART start in selected patients could be considered in settings where very close monitoring and optimal treatment are available

IRIS development in patients with previous OIs

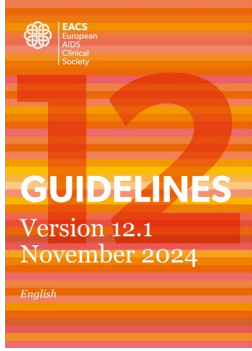
Meta-analysis of data from 54 cohorts
involving > 13,000 patients

Previous OI	Pooled %	95% CI
TB	15.7	9.7 – 24.5
Crypto meningitis	**19.5**	**6.7 - 44.8**
CMV retinitis	37.7	26.6 - 49.4
Kaposi's sarcoma	6.4	1.2 - 24.7
PML	16.7	2.3 - 50.7

4.5% (2.1-8.6) of patients with any type of IRIS died, 3.2% (0.7-9.2) of those with tuberculosis-associated IRIS died, and **20.8% (5.0-52.7) of those with cryptococcal meningitis died**.

Muller, et al. Lancet ID 2010

When to start ART in persons with Opportunistic Infections



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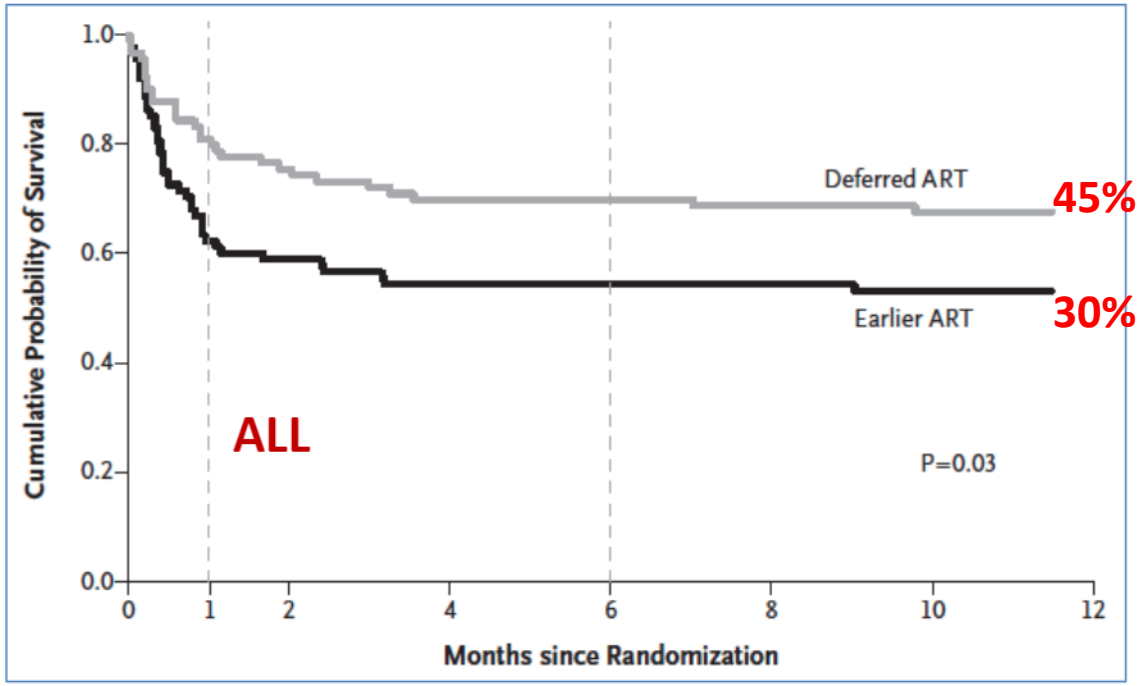
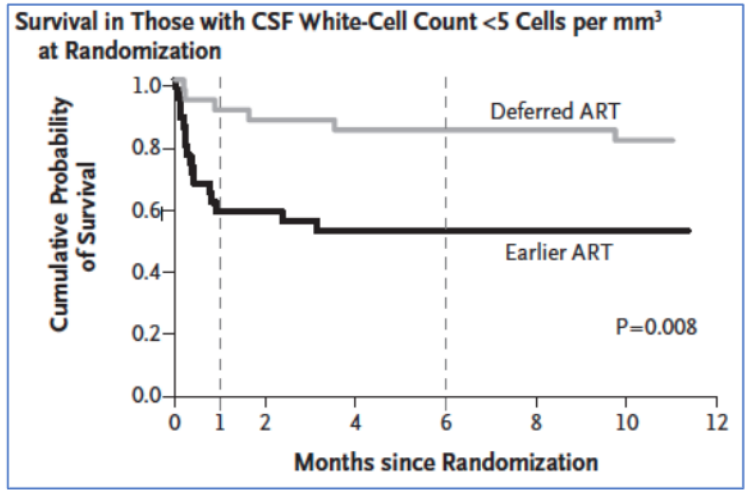
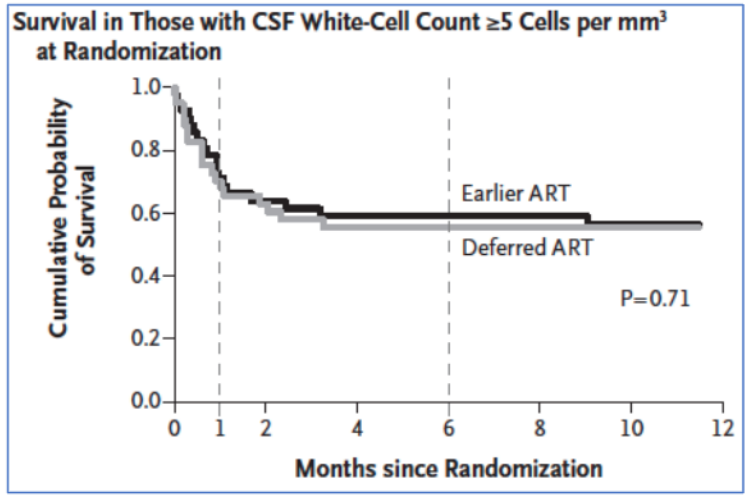
Timing of ART after diagnosis of Cryptococcal meningitis (Cryptococcal Optimal ART Timing - COAT) Trial: longer survival after deferred ART

- 177 pts, Uganda and South Africa
- **Early ART**: 1-2 weeks after dx
- **Deferred ART**: 5 weeks after dx
- Rx: amphotericin B + fluconazole
- Outcome: survival at 26 weeks





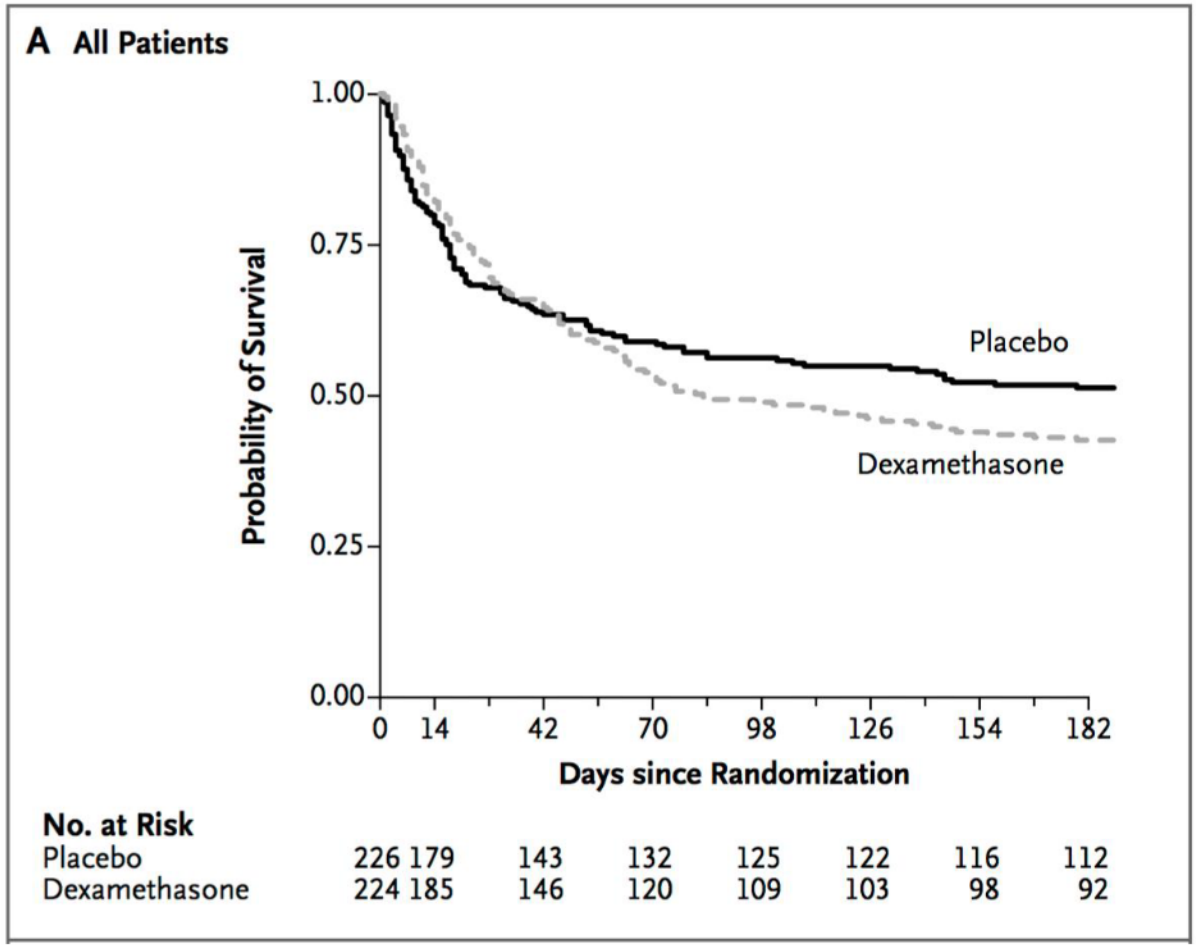
CSF WBC < 5/µL



CSF WBC > 5/µL

Boulware DR, N Engl J Med 2014

The Crypto-Dex Study: A randomised, double-blind, placebo-controlled phase III trial of adjunctive dexamethasone in HIV-CM



Deaths at 10 weeks:

- 106 of 224 (47%) in the dexamethasone group
- 93 of 226 (41%) in the placebo group

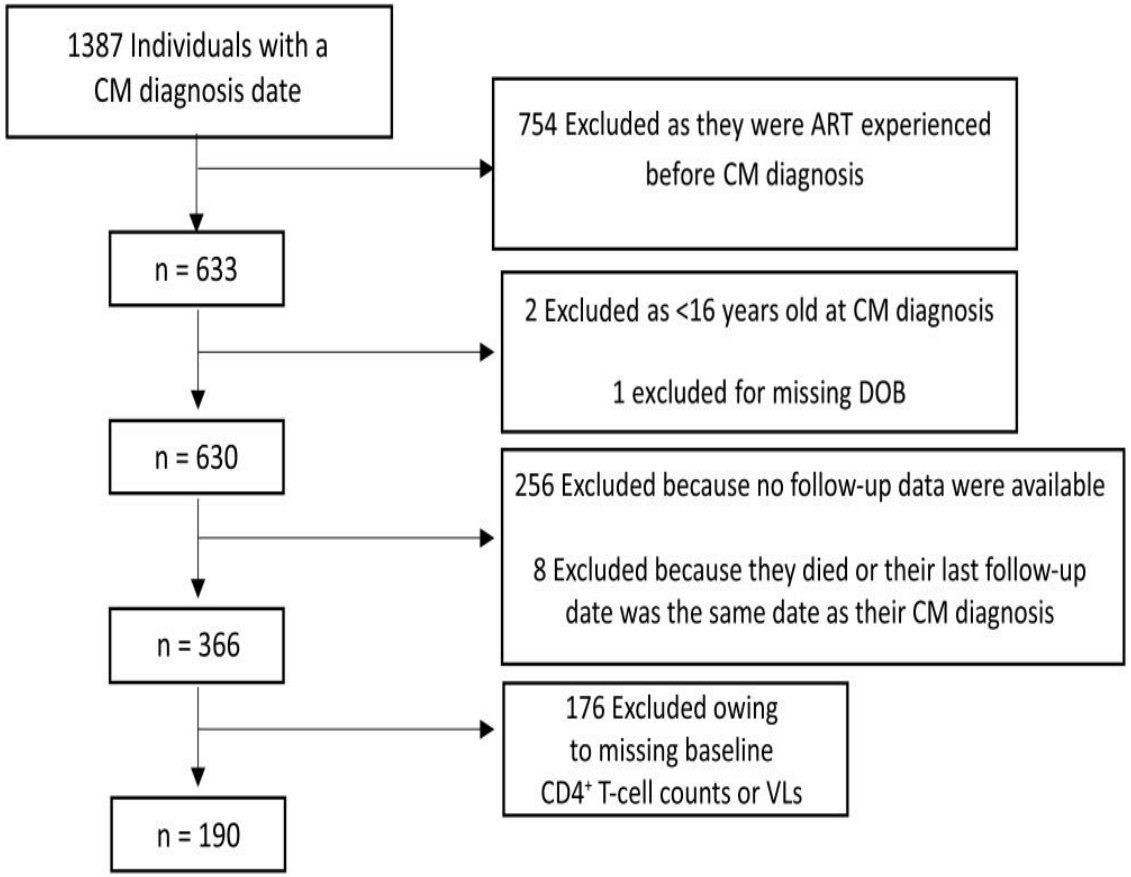
- Dexamethasone (0.3 mg/kg/day, reducing weekly over 6 weeks) did not reduce mortality among patients with HIV-CM
- It was associated with more adverse events (infections, renal and cardiac) and disability than placebo

J. Beardsley, NEJM 2016

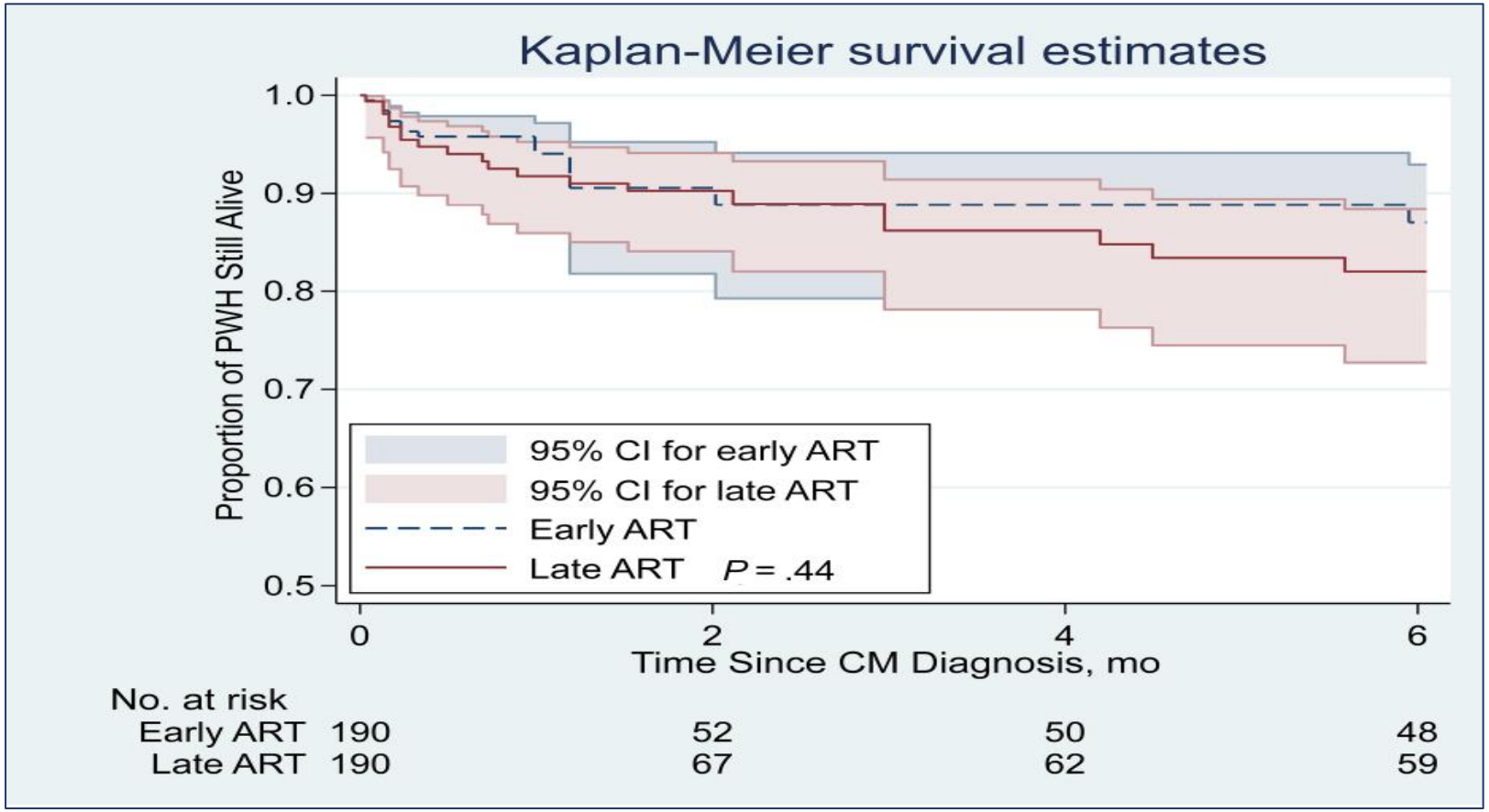
Early Antiretroviral Therapy Not Associated With Higher Cryptococcal Meningitis Mortality in People With Human Immunodeficiency Virus in High-Income Countries: An International Collaborative Cohort Study

Clinical Infectious Diseases
MAJOR ARTICLE
IDSA Infectious Diseases Society of America

Study design: Data on ART-naive PWH with CM diagnosed from 1994 to 2012 from Europe/North America were pooled from the COHERE, NA-ACCORD, and CNICS HIV cohort collaborations. Follow-up was considered to span from the date of CM diagnosis to earliest of the following: death, last follow-up, or 6 months



Estimated survival in PWH with cryptococcal meningitis (CM) according to early or late ART Initiation



Mimicking an RCT, with 190 people in each group, there were 13 deaths among participants with an early (within 14 days of CM) ART regimen and 20 deaths among those with a late (14–56 days after CM)ART regimen. The crude and adjusted hazard ratios comparing late with early ART were 1.28 (95% confidence interval, .64–2.56) and 1.40 (.66–2.95), respectively

CID 2023:77 (1 July)

Clinical Infectious Diseases

EDITORIAL COMMENTARY

Timing of Antiretroviral Therapy in Cryptococcal Meningitis: What We Can (and Cannot) Learn From Observational Data

David R. Boulware[1] and Joseph N. Jarvis[2]

[1]Department of Medicine, University of Minnesota, Minneapolis, Minnesota, USA; and [2]Department of Clinical Research, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom

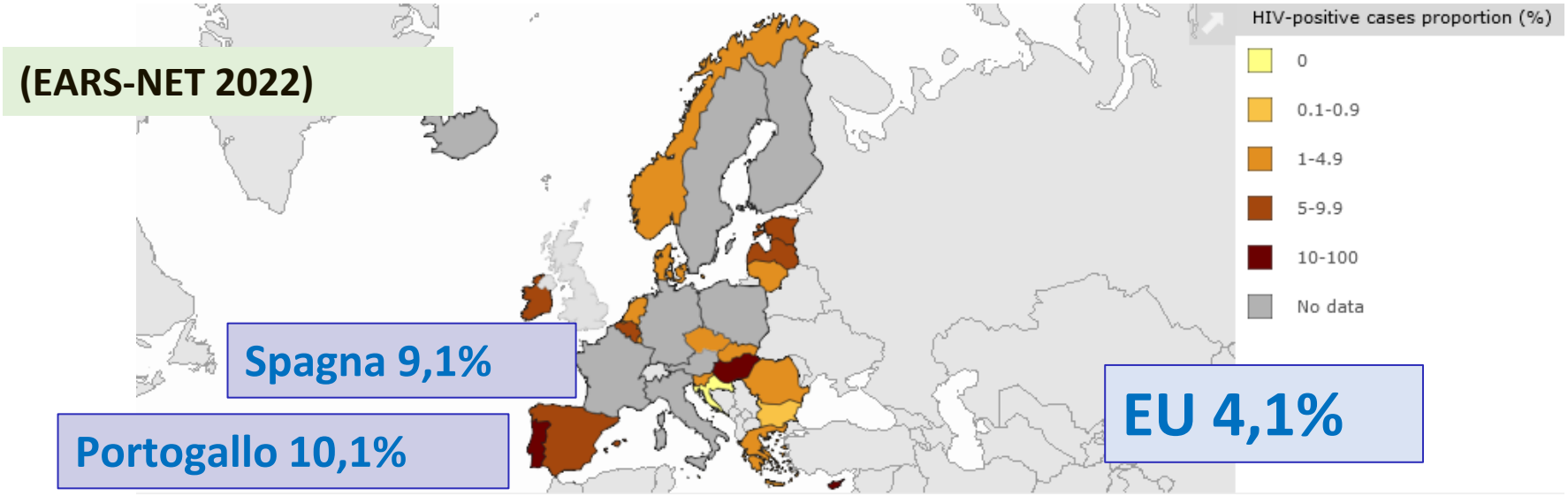
Clinical trials are difficult to conduct. Careful analysis of observational data plays an important role in informing clinical care. Mimicking clinical trials using “big data” is interesting and increasingly used; however, complex statistical methods can never overcome the limitations inherent in observational datasets, especially when large amounts of missing data exist. Small observational studies cannot replace appropriately powered randomized clinical trials. To determine whether the impact of early ART initiation in cryptococcal meningitis differs in high-income countries and whether guidelines should change, the authors would need to conduct further randomized clinical trials.

Special Considerations Regarding ART Initiation

The issue of when to start ART in the setting of cryptococcal meningitis remains controversial. The randomized trials, most of which are more than a decade old, were largely done in low- and middle- income countries where access to currently recommended antifungal treatment, monitoring, and support may have been less optimal, and they demonstrated overall mortality rates substantially higher than had been reported in higher resourced settings. While the observational cohort study in higher resourced settings is limited by its observational, retrospective nature and cannot fully address unrecognized biases, it is unlikely that a suitably powered prospective randomized trial can be done in high-resourced settings now, given the precipitous decline in incidence of cryptococcal meningitis in people with HIV treated with more effective antifungal therapy and more effective and better tolerated ART regimens than were available in some of the earlier trials. Therefore, most experts aim to start ART within 4 weeks of antifungal therapy. Therefore, most experts aim to start ART within 4 weeks of antifungal therapy; however, individual patient factors may allow for earlier or later initiation of ART. In general, ensuring that the patient's CSF cultures are sterile before starting ART will reduce the risk of IRIS. If ART must be started sooner, the patient should be monitored closely for paradoxical IRIS with a low threshold to intervene.

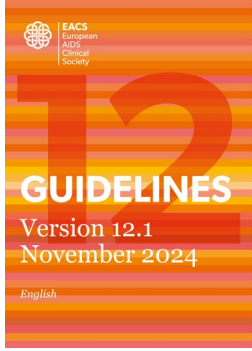
Epidemiology of TB/HIV Coinfection in Europa

- TB is the leading cause of morbidity and mortality among people living with HIV worldwide. In 2019, 820,000 HIV+ patients developed TB, and 208,000 deaths among HIV+ patients were attributed to TB.
  With the spread of ART, there has been a 1.6% per year reduction in patients with TB.



In Italy, in 2022, 2,439 cases of TB were reported (69% pulmonary) with an incidence rate of 3.8 cases per 100,000 inhabitants, a slight increase compared to 2021.
From 2012 to 2021, patients with AIDS accounted for between 8% and 13% of the total TB cases. The proportion of foreigners among AIDS/TB cases decreased from 80% in 2012 to 63% in 2021. [ISS data]

When to start ART in persons with Opportunistic Infections



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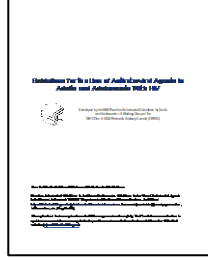
Timing of ARV in HIV/TB coinfection

STUDY	N. Patients	cART Initiation	CD4+ (median)	OUTCOME	IRIS
SAPiT 1/2 Study (South Africa) N Engl J Med 2011	642	Group 1: within 4 weeks of starting Tb Ttherpy Group2: within 4 weeks of continuation phase of TB therpy Group 3: within 4 weeks after completing tuberculosis treatment	**< 500 (150)**	56% lower mortality (HR= 0.44; p = 0.003)in Groups 1-2(5.4 per 100 person-years (25 deaths; n=429)) compared to Group 3 (12.1 per 100 person-years (27 deaths; n=213))	12.4% (53/429,) participants in Groups 1-2 and 3.8% (8/213)in Group 3
CAMELIA Study (6 CAMBODIAN centers) N Engl J Med 2011	661	Group 1: 2 weeks after TB therapy Group 2: 8 weeks afterTB therapy	**< 200** (25)	59 deaths (18%) in Group 1 vs 90 deaths (27%) in Group 2 (hazard ratio, 0.62; P=0.006)	Increased incidence in Group 1 vs Group 2(HR, 2.51; 1.78 to 3.59; P<0.001)
AIDS Clinical Trials Group Study A5221 (STRIDE) N Engl J Med 2011	809	Group 1: within 2 weeks of TB Therapy (immediate ART) Group 2: within 8–12 weeks of TB therapy (early ART)	**< 250** (77)	12.9% of AIDS/death in Group 1 by 48 weeks compared to 16.1% in Group 2 (p=0.45) 15.5% vs 26.6% when CD4<50 cell/mmc (p=0.02)	11% in Group 1 vs. 5% in Group 2: (p=0.002)

Considerations for Antiretroviral Use in People With Coinfections



Updated: September 12, 2024
Reviewed: September 12, 2024

Tuberculosis/HIV Coinfection

Panel's Key Considerations and Recommendations Regarding Tuberculosis/HIV Coinfection

Key Considerations and Recommendations

- All people with HIV and active tuberculosis (TB) who are not on antiretroviral therapy (ART) should be started on ART **(AI)** as described below.
  - **CD4 T lymphocyte (CD4) cell counts <50 cells/mm^3:** Initiate ART as soon as possible, but within 2 weeks of starting TB treatment **(AI).**
  - **CD4 counts ≥50 cells/mm^3:** Initiate ART within 2 to 8 weeks of starting TB treatment **(AI).**
  - **During pregnancy, regardless of CD4 count:** Initiate ART as early as feasible for treatment of the person with HIV and prevention of HIV transmission to the infant **(AIII).**
  - **With TB meningitis:** Initiate ART after TB meningitis is under control and after at least 2 weeks of anti-TB treatment to reduce the risk of life-threatening inflammation in a closed space as a result of immune reconstitution **(AIII).**

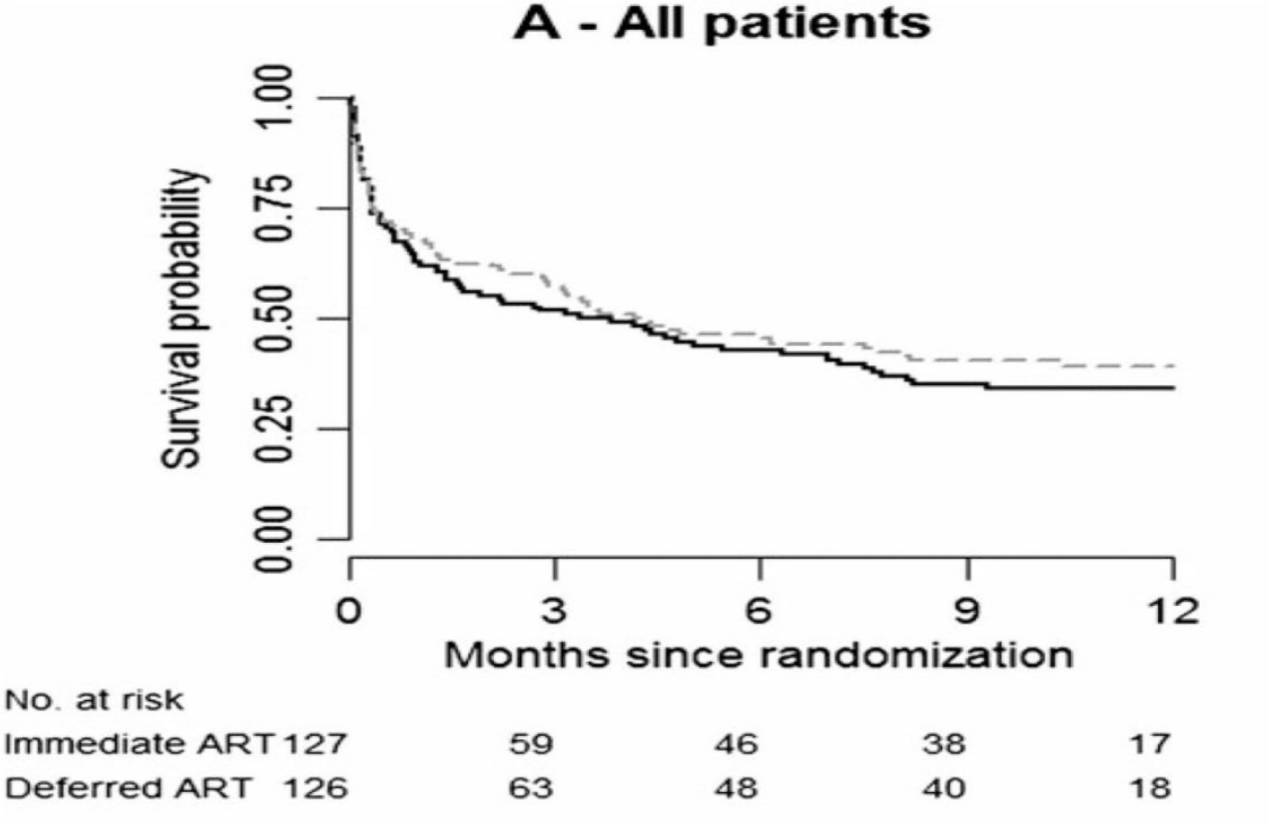
American Thoracic Society (ATS) and /Infectious Diseases Society of America (IDSA) guidelines recommend that people with TB meningitis should not start ART before 8 weeks of TB treatment is completed, regardless of CD4 count

Timing of Initiation of Antiretroviral Therapy in Human Immunodeficiency Virus (HIV)–Associated Tuberculous Meningitis

Study design: randomized, double-blind, placebo-controlled trial of immediate versus deferred (>2 months) ART in 253 patients with HIV-associated tuberculous meningitis

Results

Immediate ART was not significantly associated with 9-month mortality (hazard ratio [HR], 1.12; 95% confidence interval [CI], .81–1.55; *P* = .50) or the time to new AIDS events or death (HR, 1.16; 95% CI, .87–1.55; *P* = .31). The percentage of patients with severe (grade 3 or 4) adverse events was high in both arms (90% in the immediate ART group and 89% in the deferred ART group; *P* = .84), but there were significantly more grade 4 adverse events in the immediate ART arm (102 in the immediate ART group vs 87 in the deferred ART group; *P* = .04).



Black solid lines correspond to immediate antiretroviral therapy (ART), dashed gray lines to deferred ART

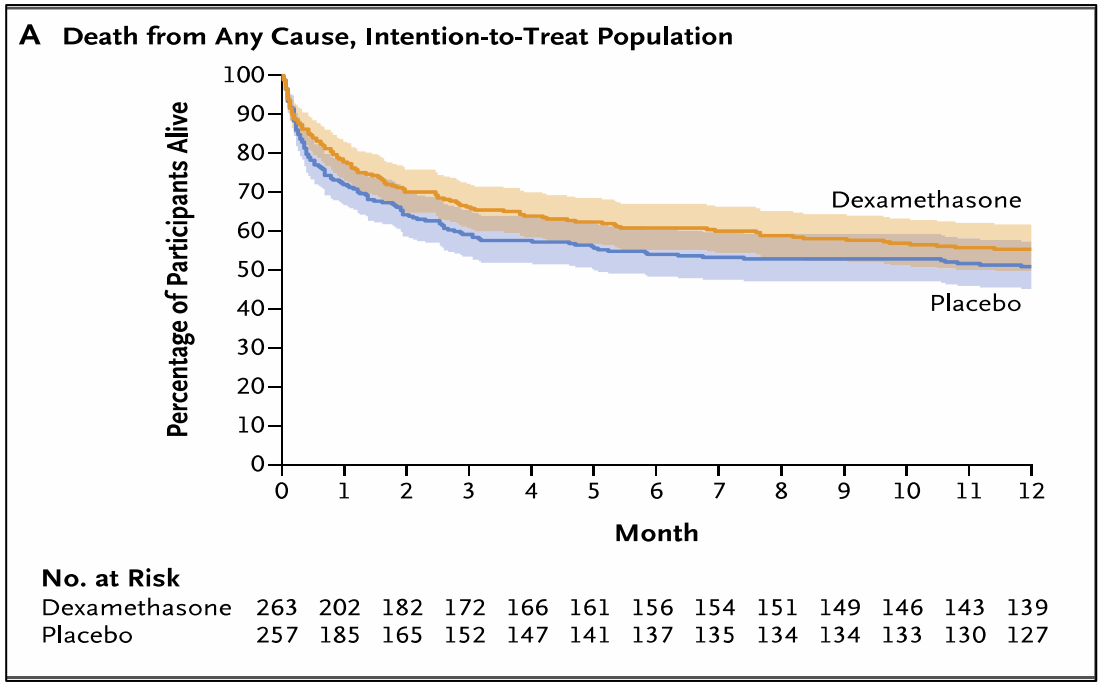
Clin Infect Dis. 2011;52(11):1374-1383.

Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults

Study design: double-blind, randomized, placebo-controlled trial involving HIV- positive adults (≥18 years of age) with tuberculous meningitis in Vietnam and Indonesia

Results: 520 adults were included. Death occurred in 116 of 263 participants (44.1%) in the dexamethasone group and in 126 of 257 participants (49.0%) in the placebo group (hazard ratio, 0.85; 95% confidence interval, 0.66 to 1.10; P=0.22).
Incidence of IRIS was similar in the two groups of patients.
No differences in incidence of serious adverse events were recorded in the two groups

Conclusion: Among HIV-positive adults with tuberculous meningitis, adjunctive dexamethasone, as compared with placebo, did not confer a benefit with respect to survival or any secondary end point.



N Engl J Med 2023;389:1357-67.

What Antiretroviral therapy to start in AIDS subjects?

Data on the efficacy of common regimens to treat advanced HIV/AIDS people are limited. Most trials have had <20% of participants with CD4 cell counts <200 cells/μL, and these trials were not powered to detect differences in this subpopulation

LAPTOP (NEAT44) – The Late Presenter Treatment Optimisation Study

An Open-Label, Multi-Centre, Randomised Study to Investigate Integrase Inhibitor Versus Boosted Protease Inhibitor Antiretroviral Therapy for Patients with Advanced HIV-Disease

SPONSOR: NEAT ID Foundation

Sponsor code: NEAT44
EudraCT: 2018-003481-13

Phase: III

Indication: ART-naïve HIV-1 infected patients

Countries: UK, France, Germany, Spain, Ireland, Ukraine, Romania & Poland

Sites: 55

Status: Ongoing, closed to recruitment

Antiretroviral regimens in TB/HIV co-infection

EACS European AIDS Clinical Society
12 GUIDELINES
Version 12.1
November 2024
English

Regimen	Main requirements	Footnotes (Additional guidance)
Recommended regimens with rifampicin		
2 NRTIs + INSTI		
TXF/XTC + DTG bid		I (tenofovir salts) II (DTG: dosing)
2 NRTIs + NNRTI		
TXF/XTC + EFV or TDF/FTC/EFV	At bed time or 2 hours before dinner	I (tenofovir salts) III (EFV: suicidality. HIV2 or HIV-1 group 0, dosing)
ABC/3TC + EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bed time or 2 hours before dinner	IV (ABC: HLA-B*57:01) III (EFV: suicidality. HIV-2 or HIV-1 group 0, dosing)
Alternative regimens with rifampicin		
2 NRTIs + INSTI		
TXF/XTC + RAL bid		I (tenofovir salts) V (RAL: dosing)
ABC/3TC + RAL bid	HBsAg negative HLA-B*57:01 negative	IV (ABC: HLA-B*57:01) V (RAL: dosing)
Other combinations with rifabutin		
2 NRTIs + PI/r		
TXF/XTC + DRV/r	With food	VI (rifabutin dosing)
ABC/3TC + DRV/r	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL With food	IV (ABC: HLA-B*57:01) VI (rifabutin dosing)

*** DTG should be dosed 50 mg bid when given with rifampicin since rifampicin lowers DTG exposure. This dose adjustment should be maintained for 2 weeks after stopping rimfampicin as the inducing effect persists after discontinuation of a strong inducer**

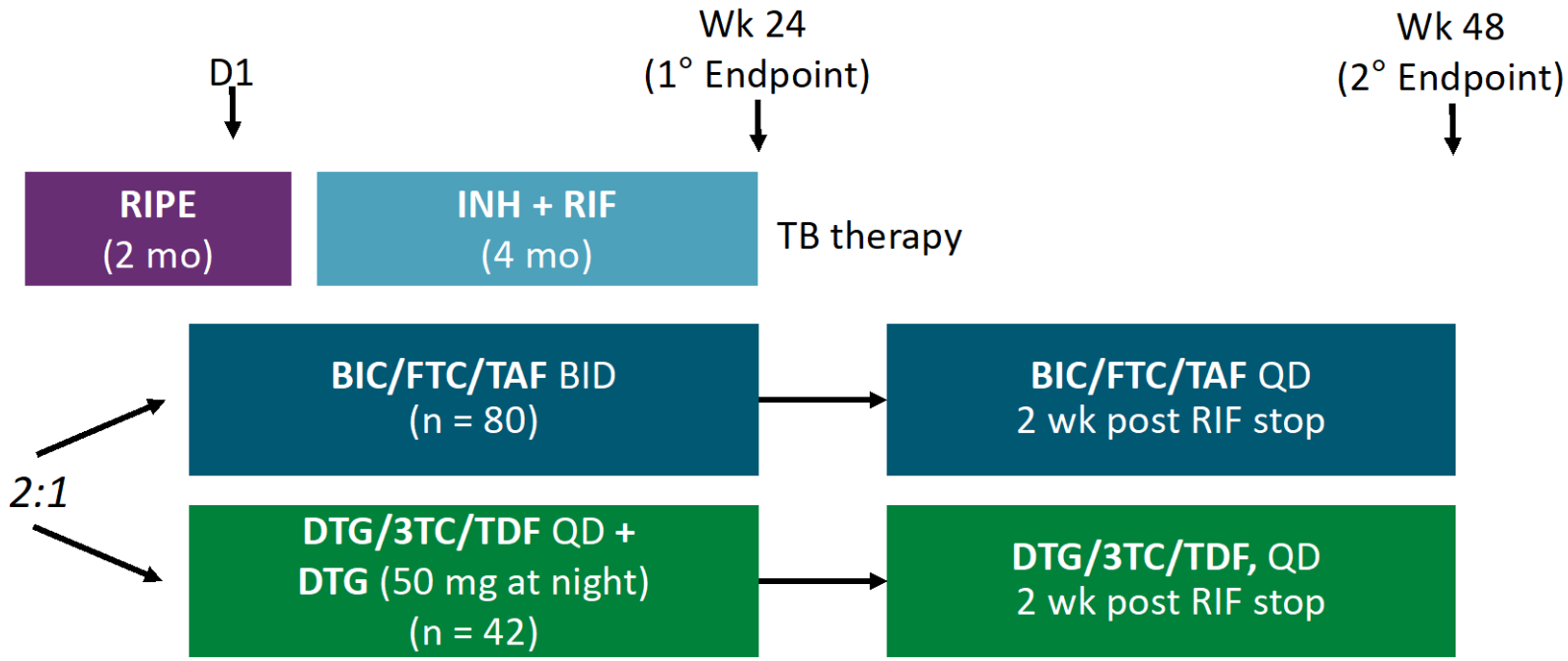
ARV and Rifampin/Rifabutin Drug-Interactions

Antiretroviral therapy	Rifampin/Rifabutin	Recomendations
Dolutegravir (50 mg x 2)	Rifampin (10 mg/kg)	**(AI)**
Dolutegravir (50 mg x 1)	Rifabutin (5 mg/kg)	**(AII)**
Efavirenz (600 mg/die)	Rifampin (10 mg/kg)	**(AII)**
Raltegravir (800 x 2)	Rifampin (10 mg/kg)	**(BI)**
Raltegravir (400 mg x 2)	Rifabutin (5 mg/kg)	**(BII)**
Lopinavir/ritonavir (800/200 mg x 2)	Rifampin (10 mg/kg)	**(BI)**
Lopinavir/ritonavir (400/100 mg x 2)	Rifabutin (2,5 mg/Kg)	**(AI)**
Doravirine (100 mg x 2)	Rifabutin (5 mg/kg)	**Expert opinion**
Rilpivirin oral (50 mg/die)	Rifabutin (5 mg/kg)	**Expert opinion**

INSIGHT: Study Design

- Open-label, noncomparative, randomized, controlled phase IIb trial in South Africa

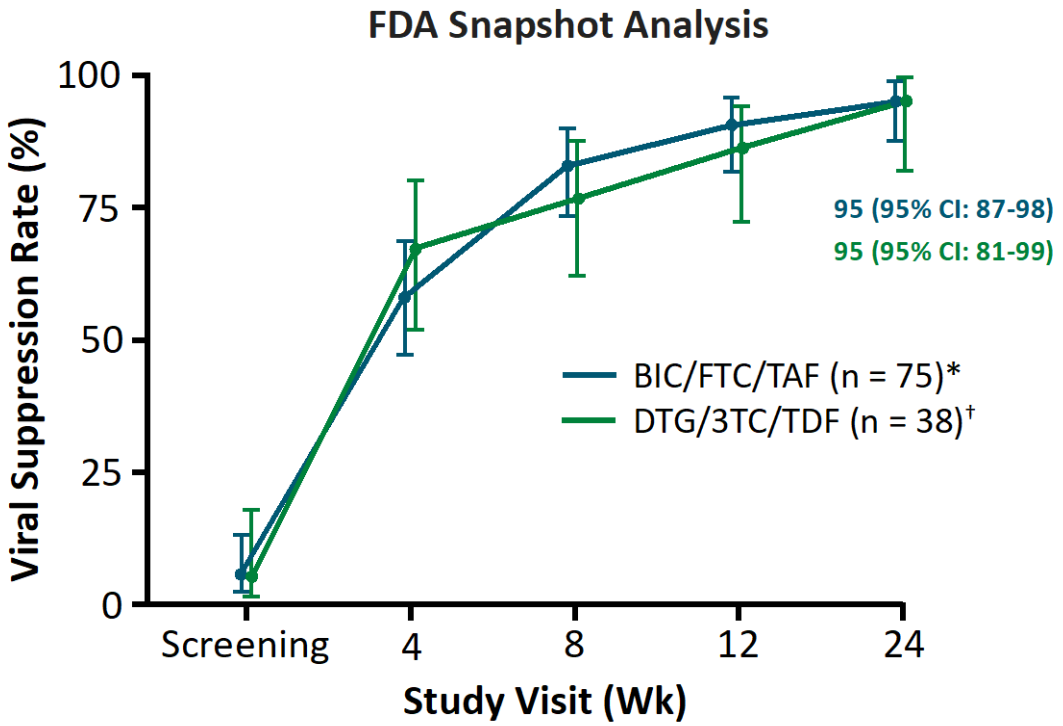
ART-naive *or* ART-nonnaive adults with HIV (no ART ≥3 mo at the time of enrollment); CD4+ ≥50 cells/µL; confirmed RIF-susceptible TB and/or on first-line RIF-based TB treatment (≤8 wk at the time of enrollment); HBsAg negative; eGFR ≥60 mL/min/1.73m^2, ALT ≤3 ULN; total bilirubin ≤2.5 ULN; Hb ≥ 7.0 g/dL (females ≥6.5g/dL); platelet ≥ 50,000/mm^3; ANC ≥650/mm^3; women on contraception (N = 122)

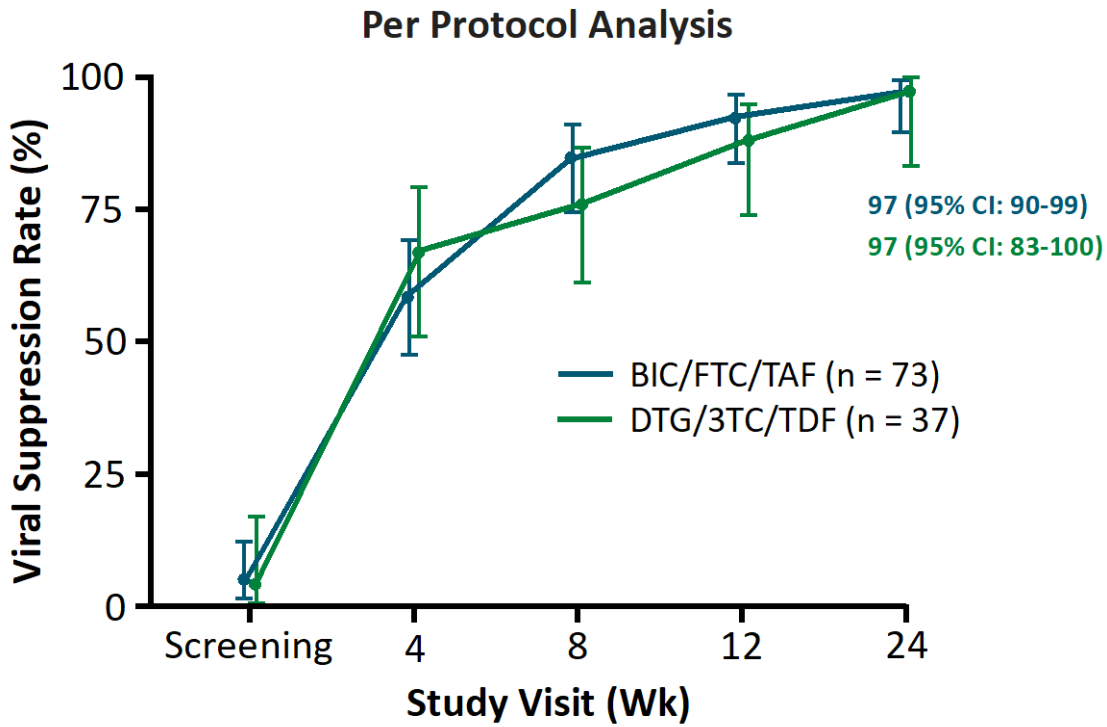


- **Primary endpoint**: viral suppression rate (HIV-1 RNA <50 copies/mL) at Wk 24 in BIC/FTC/TAF arm
- **Secondary endpoints**: viral suppression rate at 12, 24, 48 wk in DTG arm and 12, 48 wk in BIC arm; PK of BIC during and after TB therapy; safety; ART resistance mutations at Wk 24, 48; grade 3 or higher AE or SAE

Naidoo. CROI 2024. Abstr 211.

INSIGHT: Viral Suppression at Wk 24 (Primary Endpoint)





- Viral suppression high and similar in both arms, no treatment failure observed (defined as VL >400 copies/mL at Wk 24)

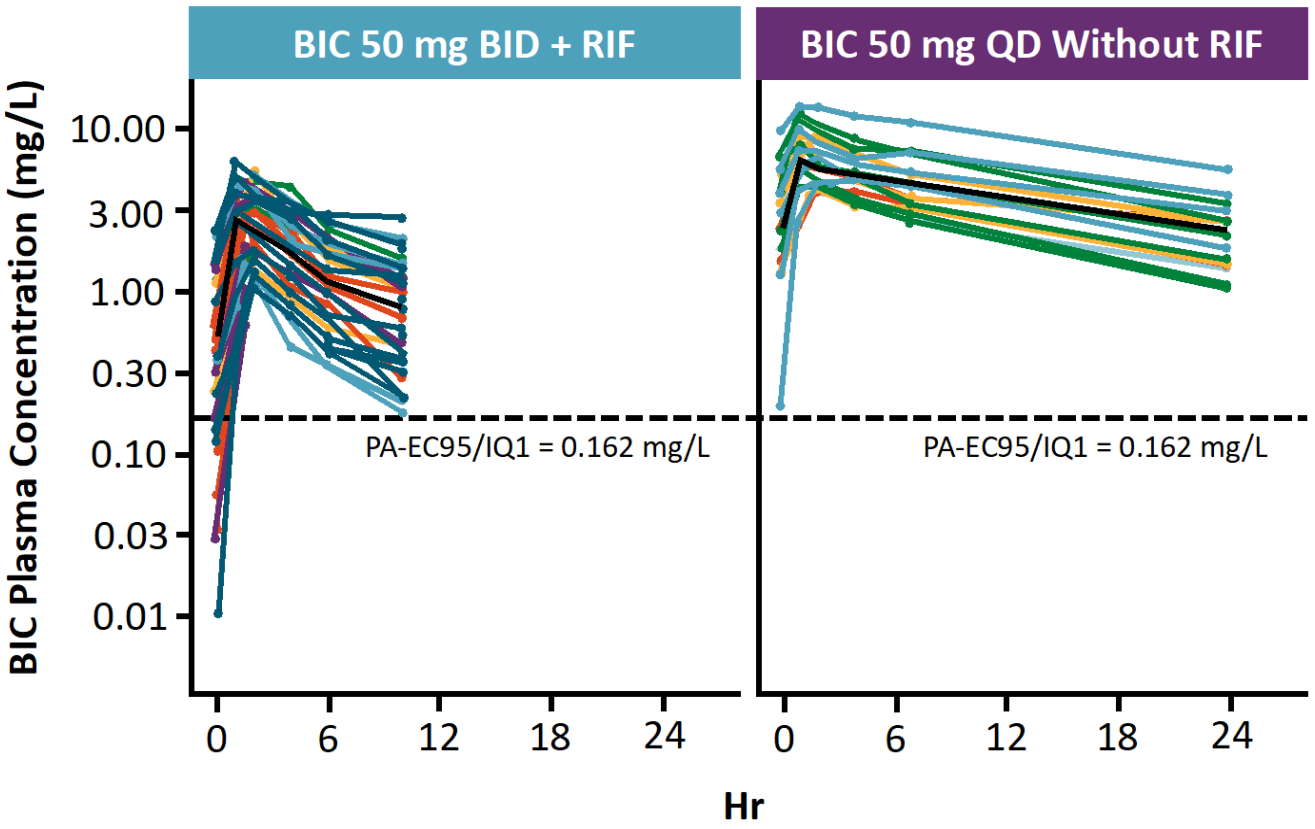
CD4+ Cells at Wk 24, cells/mm^3 (Q1; Q3)	BIC/FTC/TAF	DTG/3TC/TDF
Median CD4+ cell count	259 (213; 505)	231 (170; 311)
Median change in CD4+ cell count	96 (35; 137)	69 (27; 122)

*Early withdrawals due to relocation (n = 2).
†Death due to hemoptysis (n = 1).

Naidoo. CROI 2024. Abstr 211.

INSIGHT: BIC Pharmacokinetics During and Post-TB Treatment

Plasma Concentration of BIC for Each Individual Stratified by Dosing



BIC PK Parameter	BIC 50 mg BID With RIF at Wks 4 and 12 (n = 75)	BIC 50 mg QD Without RIF at Wk 32 (n = 22)
Trough (C_{tau}), mg/L	0.397	2.29
▪ Geometric mean (CV%)	73.4	45.1
AUC 0-24, mg*h/L	30.9	94.9
▪ Geometric mean (CV%)	42.2	35.9

- Noncompartmental analysis of semi-intensive sampling time points
- PK sampling times: pre dose 1, 2, 4, 6-8, 8-12 hr (BIC 50 mg BID with RIF); or 24-25 hr post dose (BIC 50 mg QD without RIF)
- C_{tau} calculated by extrapolation to 12 hr for BID dosing and up to 24 hr for QD dosing
- 2 participants excluded from 12 wk analysis due to levels below the limit of quantification due to nonadherence

Naidoo. CROI 2024. Abstr 211.

TN PLWH – CORIS: Cohort (Spain)

Effectiveness of B/F/TAF in PLWH With Advanced HIV

N = 232

PLWH with CD4 count < 200 cells/µL or a previous AIDS diagnosis (2019-2020) starting ART with ≥ 24 weeks' follow-up

- B/F/TAF (n = 95)
- Other ART (n = 137)

Outcome

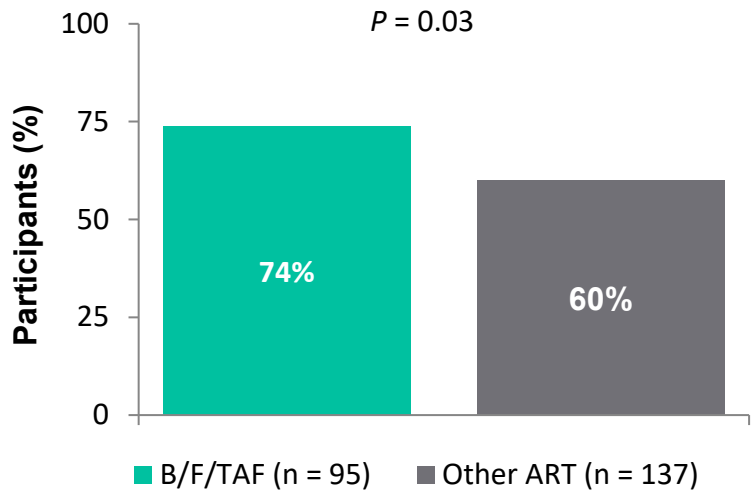
Rate of VS (HIV-1 RNA < 50 c/mL) at Week 24 with B/F/TAF (primary objective), comparison of VS rates with other regimens

2019–2020

Baseline Characteristics at ART Initiation

	B/F/TAF (n = 95)	Other ART (n = 137)
Female, %	13	15
Age, years, median	40	40
AIDS diagnosis, %	37	36
CD4 count, cells/µL, median	103	92
CD4 count < 50 cells/µL, %	23	24
HIV-1 RNA > 10^5 c/mL, %	64	62

VS (HIV-1 RNA < 50 c/mL) at Week 24



Starting ART with B/F/TAF in PLWH with advanced disease was associated with high rates of effectiveness after 24 weeks

VS, virologic suppression

Pérez-Valero I, et al. HIV Glasgow 2022, Poster P052

Antiretroviral treatment outcomes among late HIV presenters initiating treatment with integrase inhibitors or protease inhibitors

Two hundred and eighteen late presenters were included in this retrospective study: 13.8% were women and 23.8% were of non-European ethnicity, and the mean baseline CD4 count was 91 cells/μL (standard deviation 112 cells/μL). A total of 131 late presenters started on INI- and 87 on PI-based treatment. It was found that 86.1% of patients treated with INIs and 81.1% of patients treated with PIs had a viral load < 50 copies/mL at week 48; proportions of discontinuation because of adverse events were 6.1% in the INI group and 11.5% in the PI group. No significant differences in discontinuation proportions were observed at week 12 or 48 between INI- and PI-based regimens (P = 0.76 and 0.52, respectively). Virological response was equally good in those receiving INIs and those receiving PIs (86.1% vs. 81.1%, respectively; P = 0.36).

Outcome at 48 weeks	INI (*n* = 131)	PI (*n* = 87)	*P*
CD4 count (cells/μL) [median (IQR)]	360 (243.5, 461)	315 (234, 461)	0.41
CD4:CD8 ratio [median (IQR)]	0.33 (0.24, 0.43)	0.31 (0.2, 0.47)	0.68
HIV VL < 50 copies/mL* [*n* (%)]	93 (86.1)	60 (81.1)	0.36
Adverse events within the observation period [*n* (%)]	30 (24.8)	27 (32.9)	0.21
Category B diagnosis [*n* (%)]	11 (8.6)	3 (3.5)	0.17
Category C diagnosis [*n* (%)]	12 (9.4)	6 (6.9)	0.52
Mortality [*n* (%)]	3 (2.3)	3 (3.4)	0.45

HIV Medicine (2021), 22, 47--53

RAINBOW: Phase 4, single-center, single-arm study (Italy)

Efficacy and Safety of Rapid Start of B/F/TAF in Late Presenters

N = 30

ART-naïve participants presenting at HIV-1 diagnosis with advanced disease*

Outcomes

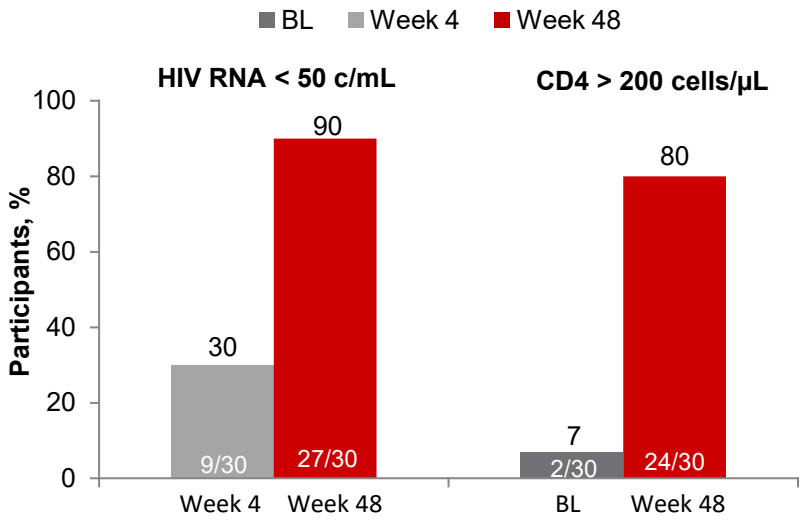
Efficacy, safety and feasibility of rapid ART initiation strategy†

May 2020–January 2021

BL Demographic and Clinical Characteristics

Characteristic	N = 30
Female sex, n (%)	5 (17)
Age, years, median (IQR)	45 (38–58)
Sexual orientation, n (%) MSM Heterosexual Other/unknown	 5 (17) 10 (33) 15 (50)
Race (White), n (%)	27 (90)
CDC disease Stage C, n (%)	13 (43)
CD4 cell count, cell/mm^3, median (IQR)	90 (39–147)
CD4/CD8 cell count, cell/mm^3, median (IQR)	0.14 (0.09–0.24)
HIV RNA at BL, $\log_{10}$ c/mL, median (IQR)	6.0 (5.4–6.4)

Rates of Virologic Suppression and CD4 Count > 200 Cells/µL



- **No ART modification** was performed once GRT was reviewed
- **2 virologic failures at Week 48, both resuppressed** on B/F/TAF

- **No ART discontinuation** due to toxicity or virologic failure
- **6** SAEs (n = 3)
- **1** participant changed ART due to disseminated TB

- **Improvement** in total cognitive performance‡

Rapid start of B/F/TAF demonstrated high rates of virologic suppression and was generally well tolerated in people with advanced HIV

*Presence of an AIDS-defining event and/or CD4 cell count < 200 cells/µL; †B/F/TAF started within 7 days of HIV diagnosis; ‡Significant improvement (P < 0.05) for memory, fine motor functioning, working memory and neuropsychological performance (NPZ 12) domains. BL, baseline; GRT, genotype resistance test; IQR, interquartile range; NPZ 12, neuropsychological test composite z score; TB, tuberculosis

Int J Antimicrob Agents . 2024 Jan;63(1):107

Comparable efficacy and safety of dolutegravir/lamivudine to a three-drug regimen among ARV naive people living with HIV with CD4 <200/mm^3: the DOLCE study

Study design: randomized, phase IV, open-label, multicentre clinical trial assessing the efficacy of DTG/3TC for the treatment of HIV-1 in treatment-naïve adults with CD4+ T-cell count ≤200 c/mm3 and HIV-1 RNA >1,000 copies/mL with no known ART-resistance or HBV co-infection, conducted in 11 sites across Argentina and Brazil

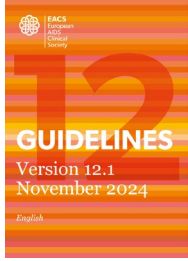
Characteristics of included patients: 25% F, 1/3 pts, CDC3, 43% pts, CD4< 117; 69% pts VL > 100.000; 23% pts, VL > 500.000; 11 PDVF with no RAMs (7 DT, 4 TT)

	Total	DT	TT	difference (95% CI)	p-value
Journal of the International AIDS Society 2024, **27(S6)**:e26370					Oral Presentati
ITT-E (global *n* = 229; TT *n* = 77; DT *n* = 152) *n* (%) [95% CI]	187 (81.7%) [76–86%]	125 (82.2%) [75–88%]	62 (80.5%) [70–88%]	2.0% (–8.7, 12.8%)	0.016
ITT-E, baseline VL >100,000 copies/ml (global *n* = 141; TT *n* = 47; DT *n* = 94) *n* (%) [95% CI]	112 (79.4%) [72–86%]	76 (80.9%) [71–88%]	36 (76.6%) [62–87%]	5.1% (–10.1, 20.3%)	0.026
Per protocol (global *n* = 204; TT *n* = 68; DT *n* = 136) *n* (%) [95% CI]	187 (91.7%) [87–95%]	125 (91.9%) [86–96%]	62 (91.2%) [81–96%]	1.8% (–6.3, 9.9%)	0.005

Efficacy analysis. Primary outcome viral load < 50 copies/ml at wk 48

Abstract Supplement HIV Glasgow 10–13 November 2024 Journal of the International AIDS Society 2024, 27(S6):e26370

Mpox



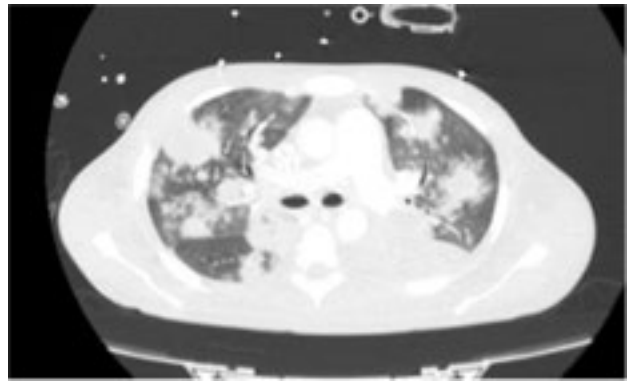
Therapeutic considerations for severe cases

Severe cases and persons at risk of severe disease should be admitted for close monitoring.

- In immunocompromised patients, it is critical to optimize immune function to maximize chances of recovery.
- To date, effectiveness of antiviral therapies in Mpox has not been systematically evaluated, and randomized trials are ongoing.
- Tecovirimat has been approved for the treatment orthopox viruses infections. Clinical trials to assess benefit of tecovirimat treatment in people with Mpox are ongoing. Administration of tecovirimat (600 md bid with fatty meal po or 200 mg bid infused over 6 hours IV for 10-14 days) may be considered in severe cases, see also MMWR-Interim clinical treatment considerations for Mpox. Tecovirimat may reduce RPV levels. Consider additional drug-drug interactions when prescribing tecovirimat; See also Anti-infective/ART interaction table
- A recent clinical trial on Mpox clade I showed that tecovirimat was safe but not effective in improving Mpox in this setting, see also NIH press release

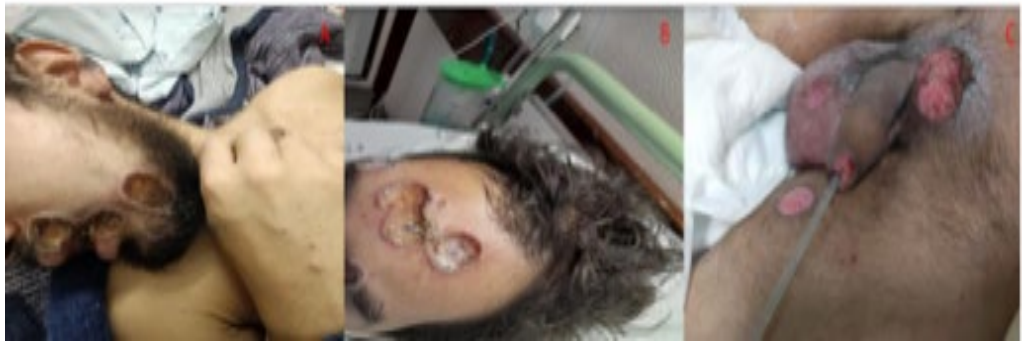
Several additional agents have been proposed as therapies for Mpox.

- Brincidofovir and cidofovir may be effective against Mpox. The use of these agents may be considered in patients not eligible to tecovirimat, or in addition to tecovirimat for severely immunocompromised individuals. Monitor closely for adverse events.
- Vaccinia immune globulin intravenous (VIGIV) can be considered for severely immunocompromised patients unable to mount an effective immune response. Caution should be applied in administering VIGIV in patients with corneal involvement. See also MMWR-Interim clinical treatment considerations for Mpox
- Topical application of trifluridine could be considered in patients with ocular involvement



Admission in tertiary hospital (Day +68)HIV viral load: 795,000 copies/mL

Regimen with intramuscular (IM) cabotegravir (CAB) and IM rilpivirine (RPV) was started on day +95, both to be administered monthly, with initial dosing of 600 mg of CAB and initiation of the later regimen, there was already a decrease in HIV viral load from 5,000,000 IV cabotegravir/rilpivirine and IV zidovudine initiation to 9010 copies/mL



Take home messages

- In high-income countries, it remains a concerning trend that the diagnosis of HIV infection is often delayed in a significant number of cases.
- .Opportunistic infections continue to pose a serious threat, as they are still associated with a notable rate of mortality. A 35% mortality rate within 5 years of diagnosis of the initial AIDS-defining opportunistic infection leaves considerable room for improvement.
- For most opportunistic infections, it is crucial that antiretroviral therapy is started without unnecessary delay. Timely initiation of this therapy can significantly improve patient prognosis and overall health.
- Specific considerations must be made regarding the initiation of antiviral therapy in the presence of cryptococcosis and tuberculosis, both due to the risk of IRIS and potential drug-drug interactions.
- Data on the efficay of common regimens to treat persons with AIDS are still scarse and further clinical studies are warrant.

Grazie per l'attenzione